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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/645,735	08/20/2003	Craig C. Mello	UMY-052DV2	9634

959 7590 08/22/2006

LAHIVE & COCKFIELD
28 STATE STREET
BOSTON, MA 02109

EXAMINER	
MONSHIPOURI, MARYAM	

ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 08/22/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/645,735	MELLO ET AL.	
	Examiner	Art Unit	
	Maryam Monshipouri	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *11 and 17-30* is/are pending in the application.

4a) Of the above claim(s) *30* is/are withdrawn from consideration.

5)☒ Claim(s) *24 and 25* is/are allowed.

6)☒ Claim(s) *11,17-23 and 26-29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *filed 7/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *see attachment*.

Applicant's response to restriction letter filed 6/29/2003 is acknowledged. Applicant elected Group I invention claims 11, 17-29 without traverse. Claim 30 is withdrawn as drawn to non-elected invention. Claims 1-10, 12-16 are canceled.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 11 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The term "high stringency" in claim 11 is indefinite. In page 11 of the specification some examples of "high stringency" conditions are provided but said examples do not specifically define the term used in claim 11.

Claim 27-28 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The term "RDE-4 mutation" in claim 27 (and its dependent claim 28) is confusing. RDE-4 in the specification is referred to as expression product of rde-4 gene. It is unclear how a polypeptide can complement a mutated "RDE-4 mutated" polypeptide.

Claim 17 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The phrase "the polypeptide of claim 11, which hybridizes ...) in claim 17 is unclear. It is indefinite as how a polypeptide can hybridize under recited

conditions. Usually, hybridization is preformed by nucleic acid sequences not by polypeptides.

Claim Rejections - 35 USC § 112

Claims 11, 17-20 and 23, 26, 27-29 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The instant invention is directed to the following genera of products that have been inadequately defined in the specification:

(1) a **genus** of polypeptides encoded by nucleic acid sequences that hybridize to the complement of SEQ ID NO:4 and their fusion products with no function.

(2) a **genus** of homologs of RDE-4 polypeptides having at least 80% identity to SEQ ID NO:4 and their fusion products with no function.

(3) a **genus** of polypeptides encoded by a DNA sequences that can complement "rde-4 mutations" with no function.

(4) a **genus** of polypeptides comprising residues 150-212 of SEQ ID NO:5 or comprising at least 30 contiguous amino acids of SEQ ID NO:3 with no function.

No functional description has been provided of the homologous sequences shown for parts 1-4 above. No information, beyond the characterization of SEQ ID NO:5 has been provided by applicants which would indicate that they had possession of the claimed genera of modified polypeptides. The specification does not contain any

disclosure of the function of all the variant polypeptide sequences derived from SEQ ID NO:5, that are within the scope of the claimed genus. Therefore many functionally unrelated polypeptides are encompassed within the scope of these claims. The specification discloses only a **single species** of each claimed genus (SEQ ID NO:5) which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Therefore, one skilled in the art cannot reasonably conclude that applicant had possession of the claimed invention at the time the instant application was filed. Since said polypeptides are inadequately described their fusion products (claims 27-28) are also inadequately described.

Applicant is referred to the revised interim guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claims 17-20, 23 and 26 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The terms "80%", "95%", "98%", and phrase "at least 30 contiguous amino acids", and "residues 150-212" in claims 17-20, 23 and 26 respectively, were not found to have support in the specification as originally filed. Hence, said terms and phrases are considered to be **new matter**. Applicant is advised to either direct the examiner to where the support for said terms and phrases are provided or possibly delete them from the claims.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –

Claims 11, 17-19, 21-23, 26-27 are rejected under 35 U.S.C. 102(b) as being anticipated by Washington University genome sequence center review (Science, 282, 2012-2018, 1998, cited in the IDS). Said review teaches a polypeptide termed as RDE-4 having 95.3% identity to SEQ ID NO:5 of this invention (see the attached alignment) as the expression product of an isolated mRNA which hybridizes to SEQ ID NO:4 under high stringency conditions, anticipating claims 11, 17-19, which inherently has both dsRNA binding motif of SEQ ID NO:8 and ds RNA binding activity (anticipating claims 21-22). Said polypeitde does comprise at least 30 residues of SEQ ID NO:5 (anticipating claim 23) and does comprise residues 150-212 of SEQ ID NO:5 by inherency, anticipating claim 26. The polypeptide of said review is also encoded by sequence that can complement "rde-4 mutation", anticipating claim 27.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 28-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Washington University genome sequence center review (cited above) in view of current recombinant protein expression and purification techniques.

As stated above, said review teaches both the mRNA encoding an RDE-4 polypeptide and the expression product thereof. Said review does not teach a fusion product of said polypeptide wherein the heterologous polypeptide can be for example a six (hexa) histidine tag.

Current recombinant protein expression and isolation techniques teach that once a gene (or mRNA) encoding a useful product is identified it is routine to insert said mRNA into an appropriate vector attached to a hexa histidine sequence tag for expressing it into a host such as E. coli. and conveniently isolating its expression product on a support which specifically binds to said hexa histidine tag.

At the time the invention was made it would have been obvious to one of ordinary skill in the art to start with the mRNA of said review and attach a hexa histidine tag to it before E. coli transformation according to current recombinant protein expression and isolation techniques.

One of ordinary skill in the art is motivated in expressing large quantities of said RED-4 encoding gene recombinantly, according to current protein expression techniques, because said review indicates that RED-4 encoding gene is an RNA interference promoting factor (which could eventually be used for cancer treatment and treating genetically inherited diseases etc.) and isolation of large quantities of said factor

(optionally attached to a histidine tag) would help in isolating RDE-4 antibodies which could be used for identification of its homologs in humans.

Finally one of ordinary skill in the art has a reasonable expectation of success in isolating RDE-4 encoding gene product attached to a hexa histidine tag because such methods of recombinantly expressing and isolating recombinant proteins are merely routine in the prior art rendering claims 27-28 obvious.

Allowable Subject Matter

Claims 24-25 are allowed because an isolated polypeptide encoded by SEQ ID NO:4 or having SEQ ID NO:5 is free of prior art. Further the prior art does not teach or suggest preparing such specifically claimed polypeptide . Hence said polypeptide is also non-obvious.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maryam Monshipouri whose telephone number is (571) 272-0932. The examiner can normally be reached on 7:00 a.m to 4:30 p.m. except for alternate Mondays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Weber Jon P. can be reached on (571) 272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only.

For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Maryam Monshipouri Ph.D.

Primary Examiner

***

27	8	2.0	466	1	SYC_RHIME	Q92r20 rhizobium m
28	8	2.0	467	2	Q7SXF0_BRARE	Q7sxf0 brachydanio
29	8	2.0	470	2	Q940V3_ARATH	Q940v3 arabidopsis
30	8	2.0	470	2	Q9ZQ54_ARATH	Q9zq54 arabidopsis
31	8	2.0	494	2	Q8QFT4_CHICK	Q8qft4 gallus gall
32	8	2.0	510	1	GUAA_AQUAE	O66601 aquifex aeo
33	8	2.0	511	2	Q6MJM1_BDEBA	Q6mjm1 bdellovibri
34	8	2.0	540	2	Q4RRT9_TETNG	Q4rrt9 tetraodon n
35	8	2.0	554	2	Q6MHB3_BDEBA	Q6mhb3 bdellovibri
36	8	2.0	589	1	SHK2_SCHPO	Q10056 schizosacch
37	8	2.0	663	2	Q4B022_9BURK	Q4b022 polaromonas
38	8	2.0	694	2	Q5AKV9_CANAL	Q5akv9 candida alb
39	8	2.0	771	2	Q7XP68_ORYSA	Q7xp68 oryza sativ
40	8	2.0	839	1	TRPV1_CAVPO	Q6r5a3 cavia porce
41	8	2.0	840	2	Q5XX15_CAVPO	Q5xx15 cavia porce
42	8	2.0	896	2	Q5QTY8_IDILO	Q5qty8 idiomarina
43	8	2.0	1098	2	Q6C905_YARLI	Q6c905 yarrowia li
44	8	2.0	1152	2	Q5P0C3_AZOSE	Q5p0c3 azoarcus sp
45	8	2.0	1188	2	O65430_ARATH	O65430 arabidopsis

Attachment

ALIGNMENTS

RESULT 1
Q22617_CAEEL
ID Q22617_CAEEL PRELIMINARY; PRT; 385 AA.
AC Q22617;
DT 01-NOV-1996, integrated into UniProtKB/TrEMBL.
DT 01-NOV-1996, sequence version 1.
DT 07-FEB-2006, entry version 36.
DE Hypothetical protein rde-4 (RNA interference promoting factor).
GN Name=rde-4; ORFNames=T20G5.11;
OS Caenorhabditis elegans.
OC Eukaryota; Metazoa; Nematoda; Chromadorea; Rhabditida; Rhabditoidea;
OC Rhabditidae; Peloderinae; Caenorhabditis.
OX NCBI_TaxID=6239;
RN [1]
RP NUCLEOTIDE SEQUENCE [LARGE SCALE GENOMIC DNA].
RC STRAIN=Bristol N2;
RX MEDLINE=99069613; PubMed=9851916; DOI=10.1126/science.282.5396.2012;
RG The C. elegans sequencing consortium;
RT "Genome sequence of the nematode C. elegans: a platform for
RT investigating biology.";
RL Science 282:2012-2018(1998).
RN [2]
RP NUCLEOTIDE SEQUENCE.
RX MEDLINE=22105477; PubMed=12110183; DOI=10.1016/S0092-8674(02)00793-6;
RA Tabara H., Yigit E., Siomi H., Mello C.C.;
RT "The dsRNA binding protein RDE-4 interacts with RDE-1, DCR-1, and a
RT DExH-box helicase to direct RNAi in C. elegans.";
RL Cell 109:861-871(2002).
CC ---
CC Copyrighted by the UniProt Consortium, see http://www.uniprot.org/terms
CC Distributed under the Creative Commons Attribution-NoDerivs License
CC ---
DR EMBL; Z30423; CAA83012.1; -; Genomic_DNA.
DR EMBL; AY071926; AAL61544.1; -; mRNA.
DR PIR; S42378; S42378.
DR Ensembl; T20G5.11; Caenorhabditis elegans.
DR WormBase; WBGene00004326; rde-4.
DR WormPep; T20G5.11; CE00630.
DR GO; GO:0005622; C:intracellular; IEA.
DR GO; GO:0003725; F:double-stranded RNA binding; IEA.
DR InterPro; IPR001159; Ds_RNA_bd.
DR Pfam; PF00035; dsrm; 2.
DR SMART; SM00358; DSRM; 2.
DR PROSITE; PS50137; DS_RBD; 2.
KW Complete proteome; Hypothetical protein.
SQ SEQUENCE 385 AA; 43408 MW; 017A9548CE9E0B2F CRC64;

Query Match 95.3%; Score 385; DB 2; Length 385;
Best Local Similarity 100.0%; Pred. No. 0;
Matches 385; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

```
Qy          1 MDLTKLTFESVFGGSDVPMKPSRSEDNKTPRNRTDLEMFLKKTPLMVLEEAAKAVYQKTP 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 MDLTKLTFESVFGGSDVPMKPSRSEDNKTPRNRTDLEMFLKKTPLMVLEEAAKAVYQKTP 60

Qy         61 TWGTVELPEGFEMTLILNEITVKGQATSKKAARQKAAVEYLRKVVEKGKHEIFFIPGTTK 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 TWGTVELPEGFEMTLILNEITVKGQATSKKAARQKAAVEYLRKVVEKGKHEIFFIPGTTK 120

Qy        121 EEALSNIDQISDKAEELKRSTSDAVQDNDNDDSIPTSAEFPPGISPTENWVGKLQEKSQK 180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 EEALSNIDQISDKAEELKRSTSDAVQDNDNDDSIPTSAEFPPGISPTENWVGKLQEKSQK 180

Qy        181 SKLQAPIYEDSKNERTERFLVICTMCNQKTRGIRSKKKDAKNLAAWLMWKALEDGIESLE 240
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        181 SKLQAPIYEDSKNERTERFLVICTMCNQKTRGIRSKKKDAKNLAAWLMWKALEDGIESLE 240
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Qy        241 SYDMVDVIENLEEAEHLLEIQDQASKIKDKHSALIDILSDKKRFSDYSMDFNVLSVSTMG 300
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        241 SYDMVDVIENLEEAEHLLEIQDQASKIKDKHSALIDILSDKKRFSDYSMDFNVLSVSTMG 300

Qy        301 IHQVLLEISFRRLVSPDPDDLEMGAEHTQTEEIMKATAEKEKLRKKNMPDSGPLVFAGHG 360
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        301 IHQVLLEISFRRLVSPDPDDLEMGAEHTQTEEIMKATAEKEKLRKKNMPDSGPLVFAGHG 360

Qy        361 SSAEEAKQCACKSAIIHFNTYDFTD 385
              |||||||||||||||||||||||||
Db        361 SSAEEAKQCACKSAIIHFNTYDFTD 385
```

RESULT 2
Q61JF8_CAEBR
ID   Q61JF8_CAEBR   PRELIMINARY;   PRT;   390 AA.
AC   Q61JF8;
DT   23-NOV-2004, integrated into UniProtKB/TrEMBL.
DT   23-NOV-2004, sequence version 1.
DT   07-FEB-2006, entry version 11.
DE   Hypothetical protein CBG09811.
GN   Name=CBG09811;
OS   Caenorhabditis briggsae.
OC   Eukaryota; Metazoa; Nematoda; Chromadorea; Rhabditida; Rhabditoidea;
OC   Rhabditidae; Peloderinae; Caenorhabditis.
OX   NCBI_TaxID=6238;
RN   [1]
RP   NUCLEOTIDE SEQUENCE [LARGE SCALE GENOMIC DNA].
RC   STRAIN=AF16;
RX   PubMed=14624247; DOI=10.1371/journal.pbio.0000045;
RA   Stein L.D., Bao Z., Blasiar D., Blumenthal T., Brent M.R., Chen N.,
RA   Chinwalla A., Clarke L., Clee C., Coghlan A., Coulson A.,
RA   D'Eustachio P., Fitch D.H.A., Fulton L.A., Fulton R.E.,
RA   Griffiths-Jones S., Harris T.W., Hillier L.W., Kamath R.,
RA   Kuwabara P.E., Mardis E.R., Marra M.A., Miner T.L., Minx P.,
RA   Mullikin J.C., Plumb R.W., Rogers J., Schein J.E., Sohrmann M.,
RA   Spieth J., Stajich J.E., Wei C., Willey D., Wilson R.K., Durbin R.,
RA   Waterston R.H.;
RT   "The genome sequence of Caenorhabditis briggsae: a platform for
RT   comparative genomics.";
RL   PLoS Biol. 1:166-192(2003).
CC   -!- CAUTION: The sequence shown here is derived from an
CC   EMBL/GenBank/DDBJ whole genome shotgun (WGS) entry which is
CC   preliminary data.
CC   ---
CC   Copyrighted by the UniProt Consortium, see http://www.uniprot.org/terms
CC   Distributed under the Creative Commons Attribution-NoDerivs License
CC   ---
DR   EMBL; CAAC01000045; CAE64977.1; -; Genomic_DNA.
DR   GO; GO:0005622; C:intracellular; IEA.
DR   GO; GO:0003725; F:double-stranded RNA binding; IEA.
DR   InterPro; IPR001159; Ds_RNA_bd.
DR   Pfam; PF00035; dsrm; 2.
DR   SMART; SM00358; DSRM; 2.
DR   PROSITE; PS50137; DS_RBD; 2.
KW   Complete proteome; Hypothetical protein.
SQ   SEQUENCE   390 AA; 43418 MW; 437178C1A2BED61D CRC64;

  Query Match   4.5%; Score 18; DB 2; Length 390;
  Best Local Similarity   100.0%; Pred. No. 9.8e-09;
  Matches   18; Conservative   0; Mismatches   0; Indels   0; Gaps   0;

```
Qy        324 GAEHTQTEEIMKATAEKE 341
              ||||||||||||||||||
Db        329 GAEHTQTEEIMKATAEKE 346
```

RESULT 3
Q5M7K6_XENTR
ID   Q5M7K6_XENTR   PRELIMINARY;   PRT;   656 AA.
AC   Q5M7K6;
DT   01-FEB-2005, integrated into UniProtKB/TrEMBL.
DT   01-FEB-2005, sequence version 1.
DT   07-FEB-2006, entry version 11.
DE   Prpf39-prov protein (Fragment).
GN   Name=prpf39-prov;
OS   Xenopus tropicalis (Western clawed frog) (Silurana tropicalis).
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC   Amphibia; Batrachia; Anura; Mesobatrachia; Pipoidea; Pipidae;
OC   Xenopodinae; Xenopus; Silurana.
OX   NCBI_TaxID=8364;
RN   [1]
RP   NUCLEOTIDE SEQUENCE.
RC   TISSUE=Embryo;
RX   MEDLINE=22388257; PubMed=12477932; DOI=10.1073/pnas.242603899;
RA   Strausberg R.L., Feingold E.A., Grouse L.H., Derge J.G.,
RA   Klausner R.D., Collins F.S., Wagner L., Shenmen C.M., Schuler G.D.,
RA   Altschul S.F., Zeeberg B., Buetow K.H., Schaefer C.F., Bhat N.K.,
RA   Hopkins R.F., Jordan H., Moore T., Max S.I., Wang J., Hsieh F.,
RA   Diatchenko L., Marusina K., Farmer A.A., Rubin G.M., Hong L.,
RA   Stapleton M., Soares M.B., Bonaldo M.F., Casavant T.L., Scheetz T.E.,